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- (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW.
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(54) Title: PHOTODYNAMIC THERAPY FOR TREATING CONDITIONS OF THE EYE

(57) Abstract: Provided are methods and compositions for the photodynamic therapy (PDT) of ocular conditions characterized by the presence of unwanted choroidal neovascularity, for example, neovascular age-related macular degeneration. The selectivity and sensitivity of the PDT method can be enhanced by combining the PDT with an anti-angiogenesis factor, for example, angiostatin or endostatin, or with an apoptosis-modulating factor. Furthermore, the selectivity and sensitivity of the PDT may be further enhanced by coupling a targeting moiety to the photosensitizer so as to target the photosensitizer to choroidal neovascularity.

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# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/04231

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K41/00 A61K38/48 A61K38/10 A61K47/48 A61P27/02

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, MEDLINE, EMBASE, BIOSIS, CHEM ABS Data, PASCAL

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99 03503 A (ALCON LAB INC ; CLARK ABBOT F (US)) 28 January 1999 (1999-01-28) claims	1-9,32
Y	WO 97 33619 A (QLT PHOTOTHERAPEUTICS INC) 18 September 1997 (1997-09-18) page 2	1-9,32
X	page 5, paragraph 2	10-12, 17-19
Y	WO 95 24930 A (MASSACHUSETTS EYE & EAR INFIRM) 21 September 1995 (1995-09-21) claims	1-9,32
X	page 5, line 16 - line 26	10-19
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Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

### \* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
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- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

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- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
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- \*8\* document member of the same patent family

Date of the actual completion of the international search

23 November 2001

Date of mailing of the international search report

05.12.01

Name and mailing address of the ISA

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# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/04231

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 98 25648 A (PHARMACYCLICS INC ; YOUNG STUART W (US); BLUMENKRANZ MARK S (US); M) 18 June 1998 (1998-06-18) cited in the application column 9, line 9 - column 10, line 19 ---	1-9,32
Y	US 5 733 876 A (FOLKMAN M JUDAH ET AL) 31 March 1998 (1998-03-31) cited in the application claims ---	1-9,32
Y	US 5 854 205 A (FOLKMAN M JUDAH ET AL) 29 December 1998 (1998-12-29) cited in the application column 4, line 4 - line 19 ---	1-9,32
Y	CIULLA T A ET AL: "CHANGING THERAPEUTIC PARADIGMS FOR EXUDATIVE AGE-RELATED MACULAR DEGENERATION: ANTIANGIOGENIC AGENTS AND PHOTODYNAMIC THERAPY" EXPERT OPINION ON INVESTIGATIONAL DRUGS, ASHLEY PUBLICATIONS LTD., LONDON, GB, vol. 8, no. 12, 1999, pages 2173-2182, XP000978671 ISSN: 1354-3784 the whole document ---	1-9,32
P,X	RENNO R Z ET AL: "Photodynamic therapy using Lu-Tex induces apoptosis in vitro, and its effect is potentiated by angiostatin in retinal capillary endothelial cells." INVESTIGATIVE OPHTHALMOLOGY AND VISUAL SCIENCE, (2000 NOV) 41 (12) 3963-71., XP000999831 abstract ---	1-9,32
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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	DIMITROFF C J ET AL: "Anti - angiogenic activity of selected receptor tyrosine kinase inhibitors, PD166285 and PD173074: implications for combination treatment with photodynamic therapy." INVESTIGATIONAL NEW DRUGS, (1999) 17 (2) 121-35., XP000999614 abstract	1-9, 32
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X	BIRCHLER M ET AL: "Selective targeting and photocoagulation of ocular angiogenesis mediated by a phage-derived human antibody fragment" NATURE BIOTECHNOLOGY, NATURE PUBLISHING, US, vol. 17, no. 10, October 1999 (1999-10), pages 984-988, XP002172061 ISSN: 1087-0156 abstract	10-19
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# INTERNATIONAL SEARCH REPORT

International Application No

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SCHMIDT-ERFURTH, U. ET AL: "Photodynamic therapy in ocular vascular disease" LASER PHYS. (1998), 8(1), 191-198 , XP000856256 abstract	10-12, 17-19
X	MILLER J W ET AL: "PHOTODYNAMIC THERAPY OF EXPERIMENTAL CHOROIDAL NEOVASCULARIZATION USING LIPOPROTEIN-DELIVERED BENZOPORPHYRIN" ARCHIVES OF OPHTHALMOLOGY, XX, XX, vol. 113, no. 6, 1 June 1995 (1995-06-01), pages 810-818, XP000672344 ISSN: 0003-9950 abstract	10-12, 17-19
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Y	HUNT, DAVID W. C. (1) ET AL: "Impact of PDT and Fas-mediated apoptosis on cells of the system." PHOTOCHEMISTRY AND PHOTOBIOLOGY, (JUNE, 1998) VOL. 67, NO. SPEC. ISSUE, PP. 69S. MEETING INFO.: 26TH ANNUAL MEETING OF THE AMERICAN SOCIETY FOR PHOTOBIOLOGY SNOWBIRD, UTAH, USA JULY 11-15, 1998 AMERICAN SOCIETY FOR PHOTOBIOLOGY. , XP001034015 abstract	20-31

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US 01/04231

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-9,32

A method of treating unwanted choroidal neovascularity in a mammal, the method comprising the steps of  
(a) administering to the mammal an anti-angiogenesis factor,  
(b) administering to the mammal a photosensitizer, (c)  
irradiating the choroidal neovascularity with laser light

2. Claims: 10-19

A method of treating unwanted choroidal neovascularity in a mammal, the method comprising the steps of  
(a) administering to the mammal a photosensitizer comprising a target moiety that binds preferentially to endothelial cells of the neovascularity, (b) irradiating the choroidal neovascularity with laser light

3. Claims: 20-31

A method of treating unwanted choroidal neovascularity in a mammal, the method comprising the steps of  
(a) administering to the mammal an apoptosis-modulating factor, (b) administering to the mammal a photosensitizer, (c) irradiating the choroidal neovascularity with laser light

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

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Information on patent family members

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